

Supplementary materials

Table S1. Data from BP enrichment analysis

Pathway	Enrichment FDR	Fold Enrichment	Genes
GO:0048511 Rhythmic proc.	9.99E-11	30.0103226	<i>GSK3B ESR1</i> <i>SIRT1 SLC6A4</i> <i>IGF1R DRD2</i> <i>DYRK1A CASP3</i> <i>NOS3 DRD3</i>
GO:0009611 Response to wounding	5.77E-12	19.2275994	<i>KNG1 IGF1</i> <i>IL6 BAX</i> <i>SLC6A4 IGF1R</i> <i>DRD2 CASP3</i> <i>CASP7 BCL2</i> <i>HMOX1 VEGFA</i> <i>NOS3</i>
GO:0009628 Response to abiotic stimulus	1.77E-12	12.3836273	<i>VEGFA IGF1</i> <i>BAX SIRT1</i> <i>SLC6A4 IGF1R</i> <i>DRD2 CASP3</i> <i>CASP7 BCL2</i> <i>FAS HMOX1</i> <i>VCP DRD3</i> <i>NOS3 GSK3B</i>
GO:1901698 Response to nitrogen compound	2.80E-10	11.2766061	<i>GSK3B DRD2</i> <i>DRD3 VCP</i> <i>SIRT1 ACHE</i> <i>SLC6A4 BCHE</i> <i>IGF1R CNR2</i> <i>IGF1 CASP3</i>

			<i>CASP7 IL6</i>
GO:0023057 Neg. reg. of signaling	2.96E-13	10.5054956	<i>GSK3B DRD2</i> <i>DRD3 ACHE</i> <i>IGF1 ESR1</i> <i>SIRT1 IGF1R</i> <i>BCL2 BAX</i> <i>SLC6A4 BCHE</i> <i>DYRK1A CNR2</i> <i>VCP HMOX1</i> <i>IL6 NOS3</i>
GO:0010648 Neg. reg. of cell communication	2.96E-13	10.4989091	<i>GSK3B DRD2</i> <i>DRD3 ACHE</i> <i>IGF1 ESR1</i> <i>SIRT1 IGF1R</i> <i>BCL2 BAX</i> <i>SLC6A4 BCHE</i> <i>DYRK1A CNR2</i> <i>VCP HMOX1</i> <i>IL6 NOS3</i>
GO:0042981 Reg. of apoptotic proc.	5.77E-12	9.75659469	<i>IGF1 FAS NGF</i> <i>CASP3 CASP7</i> <i>GSK3B BAX</i> <i>SIRT1 VEGFA</i> <i>IL6 IGF1R</i> <i>BCL2 ESR1</i> <i>HMOX1 NOS3</i> <i>KNG1 VCP</i>
GO:1901700 Response to oxygen-	1.41E-12	9.45020316	<i>GSK3B IGF1R</i> <i>DRD2 DRD3</i>

containing compound			<i>NOS3 ESR1</i> <i>SIRT1 IL6</i> <i>CASP7 ACHE</i> <i>SLC6A4 BCHE</i> <i>CASP3 BCL2</i> <i>CNR2 IGF1</i> <i>VCP HMOX1</i>
GO:0043067 Reg. of programmed cell death	7.66E-12	9.44769415	<i>IGF1 FAS NGF</i> <i>CASP3 CASP7</i> <i>GSK3B BAX</i> <i>SIRT1 VEGFA</i> <i>IL6 IGF1R</i> <i>BCL2 ESR1</i> <i>HMOX1 NOS3</i> <i>KNG1 VCP</i>
GO:0070887 Cellular response to chemical stimulus	4.21E-14	8.14708924	<i>GSK3B ESR1</i> <i>VEGFA IGF1R</i> <i>DRD2 DRD3</i> <i>IL6 SIRT1 NOS3</i> <i>CASP7 ACHE</i> <i>HMOX1 SLC6A4</i> <i>CASP3 BCL2</i> <i>CNR2 IGF1 FAS</i> <i>VCP ABCB1</i> <i>BCHE</i>
GO:0006915 Apoptotic proc.	2.27E-10	7.46011321	<i>IGF1 FAS BAX</i> <i>NGF CASP3</i> <i>CASP7 BCL2</i> <i>GSK3B SIRT1</i>

			<i>VEGFA IL6</i> <i>IGF1R ESR1</i> <i>HMOX1 NOS3</i> <i>KNG1 VCP</i>
GO:0008219 Cell death	3.40E-10	7.1855702	<i>IGF1 FAS BAX</i> <i>NGF CASP3</i> <i>CASP7 BCL2</i> <i>GSK3B SIRT1</i> <i>VEGFA IL6</i> <i>IGF1R ESR1</i> <i>HMOX1 NOS3</i> <i>KNG1 VCP</i>
GO:0023051 Reg. of signaling	4.21E-11	5.2056275	<i>GSK3B HMOX1</i> <i>IGF1 FAS NGF</i> <i>IL6 IGF1R</i> <i>DRD2 DRD3</i> <i>ACHE NOS3</i> <i>ESR1 SIRT1</i> <i>VEGFA VCP</i> <i>BCL2 BAX</i> <i>SLC6A4 BCHE</i> <i>DYRK1A CNR2</i>
GO:0010646 Reg. of cell communication	4.21E-11	5.19870144	<i>GSK3B HMOX1</i> <i>IGF1 FAS NGF</i> <i>IL6 IGF1R</i> <i>DRD2 DRD3</i> <i>ACHE NOS3</i> <i>ESR1 SIRT1</i> <i>VEGFA VCP</i>

			<i>BCL2</i> <i>BAX</i> <i>SLC6A4</i> <i>BCHE</i> <i>DYRK1A</i> <i>CNR2</i>
GO:0042221 Response to chemical	4.23E-11	4.63369708	<i>GSK3B</i> <i>ESR1</i> <i>VEGFA</i> <i>IGF1R</i> <i>DRD2</i> <i>DRD3</i> <i>NOS3</i> <i>VCP</i> <i>IL6</i> <i>ABCB1</i> <i>BAX</i> <i>SIRT1</i> <i>HMOX1</i> <i>SLC6A4</i> <i>CASP7</i> <i>BCL2</i> <i>FAS</i> <i>ACHE</i> <i>BCHE</i> <i>CASP3</i> <i>CNR2</i> <i>IGF1</i>

Table S2. Data from CC enrichment analysis

Pathway	Enrichment FDR	Fold Enrichment	Genes
GO:0035867 Alphav-beta3 integrin-igf-1-igflr complex	0.001344831	465.16	<i>IGF1</i> <i>IGF1R</i>
GO:0036454 Growth factor complex	0.001344831	232.58	<i>IGF1</i> <i>VEGFA</i>
GO:0031264 Death- inducing signaling complex	0.001344831	206.7377778	<i>FAS</i> <i>CASP3</i>
GO:0097136 Bcl-2			<i>BAX</i> <i>BCL2</i>

family protein complex	0.00136793	169.1490909	
GO:0046930 Pore complex	0.005104853	71.56307692	<i>BAX BCL2</i>
GO:0031093 Platelet alpha granule lumen	0.00136793	39.30929577	<i>IGF1 VEGFA KNG1</i>
GO:0031091 Platelet alpha granule	0.003240371	27.36235294	<i>IGF1 VEGFA KNG1</i>
GO:0045121 Membrane raft	0.005104853	11.31088146	<i>FAS SLC6A4 NOS3 IGF1R</i>
GO:0098797 Plasma membrane protein complex	0.002259423	7.492510067	<i>FAS IL6 IGF1R CASP3 IGF1 DRD2</i>
GO:0036477 Somatodendritic compartment	0.001344831	7.219778271	<i>NGF IGF1R DRD2 DYRK1A CASP3 CNR2 GSK3B</i>
GO:0098796 Membrane protein complex	0.001344831	5.608091092	<i>FAS IL6 IGF1R CASP3 VCP IGF1 BAX DRD2 BCL2</i>
GO:0045202 Synapse	0.00136793	4.68806271	<i>GSK3B SLC6A4 NGF DRD2 ACHE DRD3 CASP3 VCP CNR2</i>

GO:0030054 Cell junction	0.003438141	3.571285988	<i>GSK3B SLC6A4</i> <i>NGF DRD2</i> <i>ACHE VEGFA</i> <i>DRD3 CASP3</i> <i>VCP CNR2</i>
GO:0005615 Extracellular space	0.001344831	3.34185134	<i>FAS ABCB1</i> <i>BAX KNG1</i> <i>BCHE VCP</i> <i>IGF1 VEGFA</i> <i>NGF IL6 ACHE</i> <i>CASP7 HMOXI</i>
GO:0005576 Extracellular region	0.005104853	2.586986096	<i>FAS ABCB1</i> <i>BAX KNG1</i> <i>BCHE VCP</i> <i>IGF1 VEGFA</i> <i>NGF IL6 ACHE</i> <i>CASP7 HMOXI</i>

Table S3. Data from MF enrichment analysis

Pathway	Enrichment FDR	Fold Enrichment	Genes
GO:0004104 Cholinesterase activity	0.00057698	620.213333	<i>ACHE BCHE</i>
GO:0001591 Dopamine neurotransmitter receptor activity coupled via gi/go	0.00062855	465.16	<i>DRD2 DRD3</i>

GO:0097200 Cysteine-type endopeptidase activity involved in execution phase of apoptosis	0.00064024	372.128	<i>CASP3 CASP7</i>
GO:0004952 Dopamine neurotransmitter receptor activity	0.0007198	310.106667	<i>DRD2 DRD3</i>
GO:0051434 Bh3 domain binding	0.0007198	310.106667	<i>BAX BCL2</i>
GO:0097153 Cysteine-type endopeptidase activity involved in apoptotic proc.	0.00125389	206.737778	<i>CASP3 CASP7</i>
GO:0051400 Bh domain binding	0.00210307	155.053333	<i>BAX BCL2</i>
GO:0070513 Death domain binding	0.00229275	143.126154	<i>BAX BCL2</i>
GO:0005123 Death receptor binding	0.00532161	88.6019048	<i>NGF CASP3</i>
GO:0008083 Growth factor activity	0.00108581	22.4173494	<i>VEGFA NGF IL6 IGF1</i>
GO:0002020 Protease binding	0.00114867	21.510289	<i>BCL2 CASP3 VCP GSK3B</i>

GO:0042802 Identical protein binding	7.48E-07	5.74744646	<i>BAX HMOX1</i> <i>ACHE SLC6A4</i> <i>DRD2 DYRK1A</i> <i>VCP FAS ESR1</i> <i>SIRT1 VEGFA</i> <i>BCHE IL6</i> <i>IGF1R BCL2</i>
GO:0005102 Signaling receptor binding	0.00062855	5.25011287	<i>IGF1 VEGFA</i> <i>NGF IL6</i> <i>SLC6A4 KNG1</i> <i>IGF1R DRD2</i> <i>CASP3 VCP</i>
GO:0019899 Enzyme binding	0.00064024	4.45710801	<i>ESR1 BCL2</i> <i>SIRT1 SLC6A4</i> <i>CASP3 VCP</i> <i>FAS GSK3B</i> <i>ABCB1 HMOX1</i> <i>BCHE</i>
GO:0098772 Molecular function regulator activity	0.00308259	3.78640619	<i>IGF1 VEGFA</i> <i>KNG1 NGF IL6</i> <i>CASP3 VCP</i> <i>BCL2 ESR1</i> <i>DRD2</i>

Table S4. Data from Reactome enrichment analysis

Pathway	Enrichment FDR	Fold Enrichment	Genes
R-HSA-390651 Dopamine receptors	0.00025036	372.128	<i>DRD2 DRD3</i>

R-HSA-111459 Activation of caspases through apoptosome- mediated cleavage	0.00028699	310.106667	<i>CASP3</i> <i>CASP7</i>
R-HSA-112311 Neurotransmitter clearance	1.93E-05	279.096	<i>BCHE</i> <i>ACHE</i> <i>SLC6A4</i>
R-HSA-422085 Synthesis secretion and deacylation of Ghrelin	3.94E-05	164.174118	<i>IGF1</i> <i>BCHE</i> <i>ACHE</i>
R-HSA-111471 Apoptotic factor- mediated response	3.94E-05	146.892632	<i>CASP3</i> <i>CASP7</i> <i>BAX</i>
R-HSA-109606 Intrinsic Pathway for Apoptosis	2.87E-05	70.2128302	<i>BCL2</i> <i>CASP3</i> <i>CASP7</i> <i>BAX</i>
R-HSA-9009391 Extra-nuclear estrogen signaling	3.94E-05	51.6844444	<i>ESR1</i> <i>IGF1R</i> <i>BCL2</i> <i>NOS3</i>
R-HSA-6785807 Interleukin-4 and Interleukin-13 signaling	0.00013558	35.4407619	<i>IL6</i> <i>HMOX1</i> <i>BCL2</i> <i>VEGFA</i>
R-HSA-9755511 KEAP1-NFE2L2 pathway	0.0002386	30.0103226	<i>HMOX1</i> <i>BCL2</i> <i>GSK3B</i> <i>VCP</i>

R-HSA-109581 Apoptosis	3.94E-05	26.5805714	<i>BCL2 FAS</i> <i>CASP3 CASP7</i> <i>BAX</i>
R-HSA-5357801 Programmed Cell Death	7.99E-05	22.4714976	<i>BCL2 FAS</i> <i>CASP3 CASP7</i> <i>BAX</i>
R-HSA-9006934 Signaling by Receptor Tyrosine Kinases	3.94E-05	12.7441096	<i>NGF ESR1 IGF1</i> <i>IGF1R VEGFA</i> <i>NOS3 BAX</i>
R-HSA-2262752 Cellular responses to stress	0.00025036	8.62548344	<i>IL6 HMOX1</i> <i>BCL2 VEGFA</i> <i>GSK3B VCP</i> <i>SIRT1</i>
R-HSA-8953897 Cellular responses to stimuli	0.00025205	8.46845254	<i>IL6 HMOX1</i> <i>BCL2 VEGFA</i> <i>GSK3B VCP</i> <i>SIRT1</i>
R-HSA-162582 Signal Transduction	4.48E-09	6.3211191	<i>KNG1 NGF</i> <i>ESR1 IGF1 IL6</i> <i>IGF1R BCL2</i> <i>DRD2 VEGFA</i> <i>FAS NOS3</i> <i>CNR2 DRD3</i> <i>CASP3 GSK3B</i> <i>VCP BAX</i>